Thyroid Hormone Alterations Among Women with Posttraumatic Stress Disorder Due to Childhood Sexual Abuse

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Background: *Research on thyroid activity among male combat veterans with posttraumatic stress disorder (PTSD) has consistently shown elevations in total triiodothyronine (TT_3) and inconsistent elevations of other thyroid variables. This study is the first large scale investigation of thyroid function in women with PTSD.*

Methods: *Thyroid function was measured in 63 women with PTSD due to childhood sexual abuse (PTSD-CSA) in comparison with a community sample of 42 women without current PTSD-CSA. Clinical measures included the Clinician Administered PTSD Scale (CAPS), the Evaluation of Lifetime Stressors, the Trauma Assessment for Adults and the Beck Depression Inventory.*

Results: *Women with PTSD-CSA showed significant elevations in Total T_3 and the TT_3/free thyroxine (TT_3/FT_4) ratio, the FT_3/TT_3 ratio, and modest reductions in thyroid stimulating hormone relative to our community sample. These findings could not be explained by the influence of prior trauma, lifetime PTSD or depressive symptoms.*

Conclusions: *Altered thyroid activity, especially elevated Total T_3 levels, was found in women with PTSD associated with childhood sexual abuse.*

Key Words: PTSD, triiodothyronine, thyroid stimulating hormone, childhood sexual abuse, depression, clinician administered PTSD scale (CAPS)

This is the first report on the relationship between current posttraumatic stress disorder (PTSD) and thyroid function among women. As reviewed below all previous research has been done with male combat veterans. There are two important reasons for conducting such investigations with women. First, there is a growing body of information suggesting that gender differences may have a major impact on the differential expression of PTSD-related alterations in woman and men (Kimerling et al 2002). Second, evidence that PTSD is a risk factor for medical illnesses underscores the importance of understanding how this disorder might affect thyroid function along with other key biological systems (Schnurr and Green 2004).

As noted by Mason et al (1994), the first reported relationship between traumatic stress and hyperthyroidism dates back to 1825 when Parry described the onset of thyrotoxicosis in a woman who had been terrified when her wheel chair was accidently thrown down a flight of stairs. Subsequently, Bram (1927) reviewed a series of 3,000 cases of hyperthyroidism and reported that traumatic stress had occurred in 85% of them.

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Observations of elevated thyroid function have generally been confirmed in more rigorous research with posttraumatic stress disorder (PTSD) participants. The most robust finding in four studies involving a total of 157 male combat veterans from various conflicts has been a significant elevation in total serum triiodothyromine (TT_3) (Karlovic et al 2002; Mason et al 1994; Mason et al 1996; Wang et al 1999). Other reported thyroid alterations include elevated free T_3 (FT_3) (Karlovic et al 2002; Mason et al 1994; Wang et al 1999); elevated total thyroxine (TT_4) and thyroid binding globulin (TBG) (Mason et al 1994) and an elevated TT_3/free T_4 (TT_3/FT_4) ratio (Mason et al 1994; Wang et al 1999). These alterations in thyroid function were elevated in comparison with nonPTSD participants and, with few exceptions, have not been in the thyrotoxic range.

Because results have varied from one study to the next, it is unclear whether the consistent finding of elevated TT_3 represents excessive pituitary activity (marked by elevated TSH), excessive peripheral deiodination of T_4 to T_3 (marked by elevated TT_3/FT_4), or excessive production of T_3 by the thyroid gland itself. In addition to the endocrinological significance of these results, there is also the question of generalizability of these findings, since all studies have focused exclusively on male combat veterans. It is not known whether similar thyroid alterations are present in female participants with PTSD or whether such alterations occur among PTSD participants who were exposed to a noncombat-related traumatic event.

This report describes results from assays of thyroid function with a large cohort of women with PTSD due to childhood sexual abuse (PTSD-CSA). They were compared with a community sample of women without current PTSD. To our knowledge this is the first study of this sort.

The present report addresses several questions: 1) Compared to women without PTSD, do women with PTSD-CSA exhibit altered thyroid activity?; 2) Are the alterations sustained after controlling for trauma history and depression?; 3) Do these results replicate published findings with combat-related PTSD in men?; and 4) What, if anything, can we infer about the pathophysiological significance of such alterations?

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Methods and Materials

This study measured clinical and serum thyroid variables from women with PTSD-CSA and compared them with data obtained from a community sample of women without current PTSD.

Participants

Women with PTSD-CSA were participants in a study contrasting the efficacy of cognitive-behavioral–therapy, present-centered therapy and assignment to a wait-listed group (McDonagh-Coyle et al, in press). They were recruited from the community through a combination of newspaper, radio, television and poster advertisements seeking volunteers who believed they had experienced childhood sexual abuse and had current problems related to that abuse. Childhood sexual abuse was defined as sexual contact with a male five or more years older when the woman was under age 16; this definition is consistent with that generally used in research on CSA (Briere and Runtz 1993). A standardized telephone script provided information about eligibility, assessments, randomization and therapeutic treatment. The interviewers asked about acute psychiatric needs and therapy, current substance abuse, depression, current medication use and domestic violence. Potentially eligible women were invited to a formal in-person screening interview and informed consent session. Inclusion criteria were: age 18-65, a history of CSA, a diagnosis of current CSA-related PTSD and at least one clear memory of the childhood sexual abuse. Exclusion criteria were: pregnancy, psychotic disorders, current mania, hypomania, dissociative identity disorder, depression requiring immediate psychiatric treatment, current alcohol or drug abuse, alcohol/substance withdrawal within the past 3 months, active suicidal ideation, two or more parasuicidal behaviors during the past year, and the presence of ongoing interpersonal abuse (e.g., domestic violence, stalking, etc.).

Written informed consent was obtained from all participants after a detailed description of the study, which was approved by the Dartmouth Committee for the Protection of Human Subjects. Following this, the PTSD-CSA participants completed three structured interviews to determine eligibility. The Structured Clinical Interview for DSM-IV (SCID; First et al 1996) identified Axis I and II psychiatric conditions that were comorbid or precluded participation. The Evaluation of Lifetime Stressors (Krinsley et al 1994) provided a complete trauma history. Finally, the Clinician-Administered PTSD Scale (CAPS; Blake et al 1995; Weathers et al 2001) provided PTSD diagnosis and symptom severity. Seventy-four (74) women with PTSD were initially enrolled, but only 63 provided a valid set of thyroid measurements (see below). Participant compensation was $50.00 for the initial assessment.

As described elsewhere, one of three female clinician-investigators conducted the in-depth screening, SCID and ELS interviews. A separate group of female clinician-investigators conducted the CAPS interviews. CAPS interviewers were blind to other assessments and to study condition. Interrater reliability for CAPS PTSD diagnosis was kappa = .66, and for PTSD severity score intraclass correlation was r = .98, based on a review of 56.4% of the interviews by an independent evaluator (McDonagh-Coyle et al, in press).

While the study of PTSD treatment was underway, the decision was made to recruit a community sample of women in order to benchmark neurohormonal levels. Since women enrolled in the treatment study had to have current PTSD related to childhood sexual abuse, but could also have been exposed to other abusive and/or traumatic experiences, we saw no reason to exclude Comparison group subjects who had also been exposed to similar events. Ideally, we would have recruited a Comparison group of women who had all been exposed to CSA but who had not developed PTSD as a result of such experiences. In fact, we had attempted to do this in an earlier study (McDonagh-Coyle et al 2001) but discovered that the vast majority of women who reported CSA also met criteria for current PTSD. Since our hypotheses only concerned the relationship between current PTSD and thyroid function, we therefore decided to recruit a community sample of women who did not have current PTSD (to any type of past event), who may have had lifetime PTSD, and who may have had lifetime exposure to physical or sexual abuse, as well as to other traumatic events, at rates associated with the general population. As a result, women for the Comparison group were recruited in similar fashion as those in the treatment study, and they met the same inclusion/exclusion criteria stated previously with some important exceptions. Recruitment procedures did not explicitly mention childhood sexual abuse, and a diagnosis of current PTSD was an exclusion criterion. Lifetime PTSD was permissible. For practical and compassionate reasons, we reduced the assessment burden for Comparison group women, using less invasive methods to obtain historical and diagnostic information. Instead of the SCID, untreated depression and substance abuse were detected during the formal screening. Questions about prior treatment episodes, the use of medications, and current problems enabled detection of untreated depression and substance abuse. After complete description of the study to the participants, written informed consent was obtained. Women recruited for the Comparison group completed the Trauma Assessment for Adults (TAA; Resnick et al 1996) instead of the ELS to determine their trauma history. This assessment covers the same range of potentially traumatic events, but it does so in a less invasive and clinically relevant way than the ELS. PTSD diagnosis and symptom severity were assessed with the CAPS. Fifty-one women were initially enrolled for the Comparison group, but only 42 provided a valid set of thyroid measurements (see below). Each woman in the Comparison group received $100.00 for completing all assessments.

Serum Analyses

The same procedure was followed for both groups. A 10 mL blood sample was drawn by routine venipuncture into untreated vacutainer tubes when participants arrived at the laboratory before any additional psychological or psychophysiological assessments were carried out. Only one blood sample was obtained from each participant, as is the standard procedure in research on thyroid function (Karlovic et al 2002; Mason et al, 1994). Sampling was obtained at comparable times for both groups to control for any possible diurnal or ultradian rhythms of thyroid indices. Given the fact that circulating levels of thyroid hormones are relatively stable and do not appear to be sensitive to mild stress, we did not believe that our findings would be affected by any acute laboratory conditions (Mason 1968). Finally, there is no strong evidence of fluctuations over the menstrual cycle so the scheduling of venipuncture did not take this into consideration (Weeke and Hanson 1975).

After setting of the clot and centrifugation, serum samples were frozen (−70°C) for subsequent analyses of TT 3, FT3, TT4, and FT4, thyroxine binding globulin (TBG), and thyroid stimulating hormone (TSH). Radioimmunoassay (RIA) kits from Incstar (now DiaSorin, Inc., Stillwater, Minnesota) were used to measure serum TT4, FT4, TT3, TSH and TBG concentrations (interassay coefficients of variation were 3.7%, 4.2%, 6.0%, 4.0% and 3.0% respectively). Serum FT3 concentrations were measured by an

RIA kit from Diagnostic Products Corporation (Los Angeles, California) (interassay coefficient of variation was 2.7%). All assays were conducted by investigators who were blind to any clinical information about participants. They were carried out in the laboratories of John Mason, M.D. and Sheila Wang, Ph.D. at the National Center for PTSD, Clinical Neuroscience Division, Veterans Affairs Medical Center, West Haven, Connecticut.

Clinical Measures

All clinical measures for both PTSD-CSA and Comparison participants were obtained at the same point in the protocol following the comprehensive screening procedure and after providing informed consent.

The CAPS (Blake et al 1995) is a structured clinical interview that provides a standardized method for making current and lifetime DSM-IV diagnosis of PTSD and for determining PTSD symptom severity. The CAPS has good test-retest reliability (kappa = .90 or higher over a 2 – 3 day interval), internal consistency of the three symptom clusters (alpha = .73 – .85), convergent validity with the Mississippi Scale and the Minnesota Multiphasic Personality Inventory 2-PTSD-Keane (MMPI2-PK) Scale (r's = .70 and .84), and sensitivity and specificity (74 – 84%) using a clinical interview as criterion (Weathers et al 2001).

The SCID (First et al 1996) is a semi-structured interview used to diagnose coexisting Axis I disorders, some of which were exclusion criteria, and co-existing Axis II disorders. Interviewers followed standard instructions for omitting modules when appropriate. The CAPS replaced the PTSD module of the SCID.

We used the interview version of the ELS to assess trauma history in the PTSD-CSA group. The ELS covers a wide range of traumatic experiences, both in childhood and adulthood, and is particularly sensitive to the problems of assessment concerning sexual and physical abuse. Test-retest reliability over a two week interval (kappa = .89) and construct and convergent validity are well-documented (Corcoran et al 2000). The Trauma Assessment for Adults (Resnick et al 1996) was used to assess trauma history in the Comparison women. The TAA is a structured interview that surveys low and high-magnitude stressors as well as objective and subjective characteristics of the high-magnitude stressors.

In addition, participants completed a battery of self-report assessments including the Beck Depression Inventory (BDI; Beck et al 1988) and the Spielberger State Trait Anxiety Inventory (STAI). For the BDI score, internal consistency (alpha = .76– .95 in psychiatric populations), concurrent validity with clinical ratings (r = .55 – 96), and test/retest reliability over three weeks (r = .48 – .86) and other psychometric aspects have been reviewed by Beck et al (1988). We used the 20-item state anxiety portion of the STAI (Spielberger and Sydeman 1994). This instrument has good test-retest reliability, internal consistency, and concurrent and construct validity as reviewed in detail by Spielberger et al (1996).

Statistical Analyses

All thyroid measures were included in a one-factor multivariate analysis of variance to determine whether there were overall mean differences between the two groups when all dependent variables were considered simultaneously. Subsequent univariate t-tests were performed on each dependent variable. Independent t-tests or chi square tests were used to determine group equivalence for clinical and demographic variables. Follow-up analyses of covariance were used to test the robustness of the group effect while adjusting for demographic and clinical factors. The nonparametric Spearman's Rank Coefficient (r_s) was calculated for correlational analyses between hormonal and clinical measures because of the bimodal distribution of CAPS scores between the two groups.

We excluded results from participants reporting the use of thyroid supplements (1 comparison, 6 PTSD-CSA), or missing results for any one of TT_3, TSH and TT_3/FT_4 (7 comparison, 5 PTSD-CSA). One other Comparison participant was excluded for administrative reasons (was subsequently diagnosed with current PTSD). All demographic and clinical results reported here come from the same cohorts of women, Comparison n = 42; PTSD-CSA n = 63.

Results

Group Equivalence

The Comparison and PTSD-CSA groups were similar in age, body mass index, marital status, current employment, and percent Caucasian (Table 1). Women with PTSD-CSA had lower income and lower educational attainment than Comparison women. The PTSD-CSA group also reported significantly more use of tobacco and alcohol.

The primary clinical difference between the groups was in PTSD diagnosis. All women in the PTSD-CSA group had current PTSD, whereas none of the women in the Comparison group did. The diagnostic difference between groups was reflected by a significant difference in PTSD symptom severity measured by the CAPS (Table 1). The two groups also differed significantly in the severity of depressive (BDI) and anxiety (STAI) symptoms. These clinical differences were accompanied by a significant difference in the reported use of antidepressant medication (Table 1). There were no other significant differences in reported medications across a range of psychiatric and medical categories.

The two groups also differed in trauma history as determined by the ELS for the PTSD-CSA group and by the TAA for the Comparison group. Through selection, all women in the PTSD group (n = 63) met study criteria for childhood sexual abuse. In addition to the incidence rates reported in Table 1, the PTSD-CSA group reported an average of 3.3 types of traumatic events in their lifetime, and only three women (4.4%) reported childhood sexual abuse as their only traumatic event. The Comparison group reported an average of 2.3 types of traumatic events in their lifetime; nine women (23.8%) reported no traumatic events, seven (16.7%) reported lifetime but not current PTSD (associated with a variety of traumatic events), and four (9.5%) reported childhood sexual abuse without PTSD.

Primary Findings

Initial analysis involved a multivariate analysis of variance (ANOVA) using PTSD diagnosis as the independent variable and all ten dependent variables listed in Table 2. The overall F = 3.005, with df = 10,89 and p = .003.

As shown in Table 2, PTSD-CSA participants had significant elevations in TT_3, significant reductions in TSH, and a significant elevation in the TT_3/FT_4 ratio which indicates how much T_3 is deiodinated from T_4. The FT_3/TT_3 ratio was also reliably smaller in the PTSD group, most likely because of the significant difference in TT_3 levels.

We examined the correlations between thyroid indices and PTSD symptom severity as measured by the CAPS for participants pooled from both PTSD-CSA and Comparison groups. All corre-

Table 1. Demographic and Clinical Variables for PTSD-CSA (n = 63) and Comparison (n = 42) Groups

	Comparison		PTSD-CSA			
Variable	Mean	SD	Mean	SD	t	$p \leq$
Age (years)	42.4	12.2	39.8	9.3	1.21	.229
BMI (kg/m^2)[a]	25.6	6.1	26.8	6.8	.98	.331
CAPS Total Score	6.8	9.3	68.3	14.8	23.93	.001
BDI Total Score	4.0	4.7	18.4	8.7	9.86	.001
STAI Total Score	31.8	8.9	53.8	9.8	11.69	.001
	Count	%	Count	%	χ^2	$p \leq$
% Married[b]	26	61.9%	30	47.6%	2.07	.15
% Working	36	85.7%	51	81.0%	.40	.53
% Caucasian	40	95.2%	61	96.8%	4.34	.227
% Income ≤ $20k	11	26.2%	37	58.7%	10.75	.001
% ≤ GED Education	2	4.8%	13	20.6%	5.19	.023
% Tobacco Use	0	.0%	17	27.0%	13.52	.001
% Alcohol Use	1	2.4%	14	22.2%	8.10	.004
% Contraceptive Use[c]	8	19.0%	7	11.1%	1.30	.26
% Estrogen Supplements	8	19.0%	7	11.1%	1.30	.26
% Anti-Depressant Use	3	7.1%	23	36.5%	11.66	.001
% Child Sexual Abuse	7	16.7%	63	100.0%	78.75	.001
% Child Physical Abuse	0	.0%	49	77.8%	61.25	.001
% Adult Sexual Abuse	9	21.4%	33	52.4%	10.06	.002
% Adult Physical Abuse	10	23.8%	41	65.1%	17.8	.001

Participants who were taking thyroid supplements were not included in these analyses. CAPS, Clinician Administered PTSD Scale; BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; PTSD, post traumatic stress disorder.

[a]body mass index, lbs × 703/height^2.

[b]living as married

[c]oral contraceptive use.

lations were positive, and they were highly significant for both TT_3 and TT_3/FT_4 in relationship to total CAPS scores (r_s = .29, p = .002 for TT_3 and r_s = .28, p = .004 for TT_3/FT_4; all n's = 105). For both TT_3 and TT_3/FT_4 correlations with CAPS Re-experiencing, Avoidant/Numbing and Hyperarousal subscale scores were also significant. TSH levels were negatively, but not significantly, correlated with the total CAPS and with all three CAPS subscale scores. In addition, within-group correlations between thyroid measures and CAPS scores were not significant for either the PTSD-CSA or Comparison groups.

Table 2. Thyroid Variables for PTSD-CSA (n = 63) and Comparison (n = 42) Group.

Variable	Group	Mean	SD	t	$p \leq$	Effect Size
Total T_4 (μg/100mL)	PTSD	8.24	1.59	.02	.98	.00
	Comp.	8.24	1.49			
Free T_4 (ng/100mL)	PTSD	1.28	.21	.59	.56	.12
	Comp.	1.30	.23			
Total T_3 (ng/100mL)	PTSD	158.71	26.41	4.04	.001	.80
	Comp.	138.60	22.72			
Free T_3 (pg/mL)	PTSD	2.72	.53	1.43	.16	.28
	Comp.	2.58	.42			
TBG (μg/mL)	PTSD	32.60	8.54	.50	.62	.10
	Comp.	31.81	6.60			
TSH (μIU/mL	PTSD	1.45	.72	1.96	.05	.39
	Comp.	1.76	.90			
TT_3/FT_4	PTSD	126.93	28.60	2.91	.004	.58
	Comp.	110.16	29.39			
FT_3/FT_4	PTSD	2.17	.49	1.50	.14	.30
	Comp.	2.03	.45			
FT_4/TT_4	PTSD	.16	.04	.09	.93	.00
	Comp.	.16	.03			
FT_3/TT_3	PTSD	.017	.003	2.35	.021	.47
	Comp.	.019	.003			

T3, Triiodothyronine; T4, Thyroxine; TBG, Thyroid Binding Globulin; TSH, Thyroid Simulating Hormone; PTSD, posttraumatic stress disorder; CSA, Childhood sexual abuse; Comp, Comparison group.

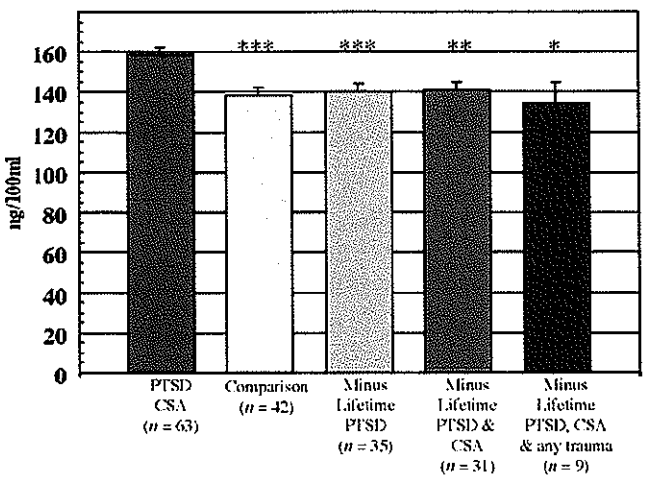

Figure 1. Total T_3 (Mean ng/100 mL ± SEM) for the PTSD-CSA and Comparison Groups. Three subsets of the Comparison Group are also shown with certain subjects subtracted from the analyses as noted. PTSD, posttraumatic stress disorder; CSA, childhood sexual abuse. * $p = .01$, ** $p = .002$, *** $p = .001$.

Follow-up Analyses

Further analyses focused on which of the significantly different demographic and clinical variables in Table 1 might have contributed to the association between PTSD diagnosis and TT_3, TSH and TT_3/FT_4 ratio. Analysis of covariance which included BDI score, antidepressant use, alcohol and tobacco use and education level yielded a significant effect only for the presence or absence of PTSD on TT_3 ($F = 6.12$. $p = .015$) and TSH ($F = 5.08$, $p = .026$), but not the TT_3/FT_4 ratio ($F = .57$, $p = .45$; all $df = 1, 98$).

Since the Comparison Group included women with lifetime (but not current) PTSD, lifetime CSA (with no history of current/lifetime PTSD) and lifetime exposure to other (nonCSA) traumatic events, we used a series of "eliminative" analyses to further examine the impact of lifetime PTSD, CSA and other previous traumatic events on thyroid variables. As shown in Figure 1, TT_3 remained lower in the Comparison group, even when seven Comparison participants with a history of lifetime PTSD ($n = 98$, $t = 3.42$, $p = .001$) and an additional four with a history of CSA without PTSD ($n = 94$, $t = 3.17$, $p = .002$) were eliminated from the analysis. In fact, when all 33 Comparison women with a history of lifetime PTSD or any child or adult trauma were eliminated, serum TT_3 for the Comparison group remained significantly lower ($n = 72$, $t = 2.54$, $p = .01$). Results are similar for TT_3/FT_4 which remained significantly lower for Comparison participants after elimination of women with lifetime PTSD ($n = 98$, $t = 2.11$, $p = .04$) and lifetime PTSD and CSA ($n = 94$, $t = 2.04$, $p = .04$) but not for lifetime PTSD and any child or adult trauma ($n = 72$, $t = 1.69$, $p = .096$). Finally, the trend is similar (but in the opposite direction) for TSH with the mean TSH higher for Comparison participants than for PTSD-CSA, but the group differences in TSH are not significant after elimination of Comparison participants with lifetime PTSD, CSA and any child or adult trauma.

Next, we considered whether the higher incidence of alcohol and tobacco use in the PTSD-CSA group might have contributed to altered thyroid function. When self-reported users of alcohol and tobacco were excluded from the analysis (one Comparison and twenty-seven PTSD-CSA women), leaving n's of 41 vs. 36 the group differences remained significant for TT_3, TSH and TT_3/FT_4 levels.

We then considered whether the higher incidence of depression in the PTSD-CSA group might have been responsible, at least in part, for the pattern of thyroid variable differences. We divided the PTSD-CSA group into nondepressed (those with BDI scores ≤ 20, $n = 41$) and depressed (those with BDI ≥ 21, $n = 22$). Analyses of variance indicated that the presence of depressive symptoms actually tended to eliminate rather than increase the differences between PTSD-CSA and Comparison participants (Table 3). PTSD participants with depression (BDI ≥ 21) tended to have lower TT_3, higher TSH and similar TT_3/FT_4 ratios compared to their less depressed (BDI ≤ 20) counterparts. Within the PTSD-CSA group only, use of antidepressants had no significant effects on TT_3, TSH or TT_3/FT_4.

The high reported incidence (see Table 1) of childhood (77.8%) and adult (65.1%) physical abuse as well as adult sexual abuse (52.4%) in the PTSD-CSA group prompted several follow-up analyses using these indicator variables as second factors in separate ANOVA designs. Neither adult sexual abuse nor adult or child physical abuse, had significant impacts on the relationship between PTSD-CSA and serum TT_3, TSH and TT_3/FT_4 ratios.

Discussion

Do Women with PTSD-CSA Exhibit Altered Thyroid Function?

This study shows that serum thyroid indices in women with current PTSD-CSA differ significantly from a nonPTSD group.

Table 3. Thyroid Variables: Comparison Group Versus PTSD-CSA Group with High (BDI ≥ 21) Versus Low (BDI ≤ 20) Depressive Symptoms

	Comparison		PTSD-CSA					Effect
Measurement	n	Mean ± SD		n	Mean ± SD	t	$p \leq$	Size
Total T_3	42	138.60 ± 22.72	Total	63	158.71 ± 26.41	4.04	.001	.80
			High BDI	22	151.00 ± 27.71	1.922	.059	.51
			Low BDI	41	162.85 ± 25.05	4.623	.001	1.02
TSH	42	1.76 ± .90	Total	63	1.45 ± .72	1.96	.045	.39
			High BDI	22	1.70 ± .79	−.293	.77	.08
			Low BDI	41	1.32 ± .65	2.025	.047	.54
TT_3/FT_4	42	110.16 ± 29.39	Total	63	126.93 ± 28.60	2.91	.004	.58
			High BDI	22	127.00 ± 27.07	2.236	.029	.59
			Low BDI	41	126.89 ± 29.72	2.579	.012	.57

ANOVAS for Comparison versus PTSD-CSA + BDI ≥ 21 versus PTSD-CSA + BDI ≤ 20 as follows: F for $TT_3 = 9.98$, $p < .001$; F for TSH = 3.59, $p = .03$; F for $TT_3/FT_4 = 4.20$, $p = .02$; all $df = 2,102$.

BDI, Beck Depression Inventory; T_3, Triiodothyronine; T_4, Thyroxine; TSH, Thyroid Stimulating Hormone; TT_3, Total Triiodothyronine; FT_4, Free Thyroxine; PTSD, posttraumatic stress disorder; CSA, childhood sexual abuse.

The major findings were significant elevations in TT_3, TT_3/FT_4, FT_3/TT_3 and significant reduction in TSH.

Are These Alterations Maintained after Controlling for Trauma History and Depression?

We conducted several follow-up analyses of group differences in thyroid indices to address plausible rival hypotheses. First we eliminated various women from the Comparison group in order to remove the influence of prior trauma and lifetime PTSD. The results were unchanged. Second, in order to determine the possible contribution of depression, we divided the PTSD-CSA group into those with none/low vs. moderate/severe depressive symptoms. Here we found that increased levels of depressive symptoms were associated with lower T_3 levels and therefore not responsible for the significant elevation of TT_3 in the PTSD-CSA group. This finding is consistent with the reported association between depression and decreased TT_3 (Joffe et al 1985; Sagud et al 2002; Wang and Shin 1989). Instead of contributing to the elevation of TT_3 in women in the PTSD-CSA group, our results suggest that depressive symptoms actually reduce the positive association between PTSD-CSA and elevated TT_3.

It is of interest that among women with premenstrual dysphoric disorder (PMDD), those with a previous history of (child or adult) sexual abuse exhibited elevated TT_3, TT_3/FT_4, FT_3/FT_4, TBG and TSH. Abused and nonabused PMDD women did not appear to differ with regard to PTSD symptoms (Girdler et al 2004). Although there are differences in the specific thyroid alterations observed in that study in comparison with our results, there is sufficient overlap to raise the question of sexual abuse per se as a predictor of elevated thyroid activity. In our results, however, there was no evidence that either previous sexual abuse (without current PTSD) or lifetime PTSD predicted altered thyroid activity.

Do These Results Replicate Published Findings with Combat-Related PTSD in Men?

For the most part, these results are consistent with previous reports on elevated TT_3 and TT_3/FT_4 detected among four different cohorts of male combat veterans (Karlovic et al 2002; Mason et al 1994, 1996; Wang and Mason 1999). Therefore, it appears that PTSD-related thyroid abnormalities are neither gender specific nor trauma specific (e.g., combat vs. noncombat). The most notable difference concerns TSH which was reduced in our PTSD-CSA participants but was no different from control participants in all studies with male veterans.

Can We Infer Anything About the Pathophysiological Significance of These Abnormalities?

The TSH result is of interest but its physiological significance is unclear. This is because one would expect free, not total T_3, to affect pituitary release of TSH. However, we found no difference in FT_3 between PTSD-CSA and Comparison subjects. These findings need to be replicated with additional female and male cohorts. Better characterization of hypothalamic-pituitary-thyroid system dynamics will require data from provocative tests with both TSH and thyroid releasing hormone (TRH). The only two published studies to date, both with male combat veterans, have had conflicting findings. One reported a blunted response to TRH among PTSD participants (Reist et al 1995). A second study found that PTSD participants resembled controls and both PTSD and control participants exhibited a greater TSH response to TRH than depressed participants (Kosten et al 1990).

From the perspective of physical health, these findings add to the growing literature suggesting that pathophysiological alterations associated with PTSD constitute a risk factor for medical illness (Schnurr and Green 2004). In this regard, it is noteworthy that whereas thyroid function is decreased among individuals with depression or chronic stress syndrome, it appears to be increased among both men and women with PTSD (Friedman and McEwen 2004).

Our findings of a positive correlation between TT_3 and CAPS scores when all participants were pooled from both the PTSD-CSA and Comparison groups is consistent with Wang and Mason (1999) who found significant correlations between PTSD symptom severity and TT_3 and FT_3 among a pooled sample of World War II male veterans with and without PTSD. A notable difference between their results and ours was that TSH was elevated in that study, in contrast to the significant reduction in TSH observed with our female participants. Our correlational finding is not consistent, however, with Wang et al (1995) who reported a positive correlation between total CAPS score and TT_3 within a male Vietnam veteran PTSD group. As stated above, within group correlations were not significant in the present study.

To summarize, elevated TT_3 appears to be a consistent finding among both men and women with combat- and CSA-related PTSD, respectively. Neither depression nor prior trauma history accounts for these findings. The pathophysiological significance of this alteration remains to be determined.

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